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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/482,585	01/13/2000	David G. Hangauer JR.	19226/931 (R-5495)	7206

7590 01/29/2003

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EXAMINER
FRIEND, TOMAS H F

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
file copy	09/482,585	HANGAUER ET AL.	
	Examiner	Art Unit	
	Tomas Friend	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,13-20 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,13-20 and 22* is/are rejected.

7)☒ Claim(s) *5 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

Change of Art Unit Designation

Please note: The Art Unit location of this application in the PTO has changed from Art Unit 1627 to Art Unit 1639. To aid in matching papers to this application, all further correspondence regarding this application should be directed to **Group Art Unit 1639**.

Status of the Application

Receipt is acknowledged of a response to an office action including an amendment on 29 March 2002 (Paper No. 14).

Status of the Claims

Claims 1-69 were pending in the application. Claims 9-12, 21, and 23-69 were cancelled in Paper No. 14. Claims 1-8, 13-20, and 22 are pending and examined on their merits.

Withdrawn Rejections

1. All outstanding rejections are withdrawn in response to applicants' amendment and arguments.

New Objections to the Specification

2. Pages 5 and 39 of the specification are objected to because they disclose structures that include pentavalent carbon atoms (see R_4).

New Objections to the Claims

3. Claims 5 and 8 are objected to for depending from rejected claims.

New Grounds of Rejection – 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-4, 6, 7, 15-20, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Cantley et al. US Patent 5,532,167 (July 1996).

Applicants' claimed invention is a method for identifying inhibitors of protein tyrosine kinases (EGF and $pp60^{c\text{-}src}$ as examples) and serine-threonine kinases (CDK kinase, for example) that do not inhibit ATP binding to the protein kinase comprising the method steps of [1] covalently attaching at least one first module comprising two or more of a hydroxyl, carboxylate, or amide to a peptide scaffold, [2] identifying which functional groups of the first module preferentially bind catalytic residues of the kinase, [3] covalently attaching at least one first module to at least one second non-peptide scaffold module that comprises an indole, [4] adding one or more specificity side chain elements to the combination of first and second modules, [5] screening for one or more combinations of first and second modules for protein kinase inhibition, and [6] selecting combinations of the first and second modules that inhibit protein kinase activity.

The '167 reference discloses methods for determining amino acid sequence motifs for Tyr and Ser-Thr kinases including the EGF receptor, $pp60^{c\text{-}src}$, and CDK2 (abstract and columns 3 and 4). The amino acid sequence motifs can be used to make pseudosubstrates and peptide analogs that inhibit protein kinases (columns 3, 5, and 21). Peptide libraries are peptide (scaffolds) with various functional groups (R groups or amino acid residues) covalently attached.

Accordingly, functional groups on the amino acid side-chains and/or amino acid residues are first modules according to the present specification. Peptide libraries are screened to determine what peptide sequences (i.e. what first modules on a peptide scaffold) are substrates for (i.e. preferentially bind to the catalytic site of) a particular kinase. As an example, the sequence near the bottom of table 8 (LYDYESWI) includes functional groups such as OH on Y and S, and carboxylate on D, while the sequence above it includes N with an amide. The W residue comprises an indole and could also be considered a second non-peptide module to which first modules comprising functional groups are added. Column 22 discloses that one or more amino acids of the substrate binding peptides may be covalently attached to a tyrphostin, which is comprised of an indole and is competitive of the substrate and not ATP. Thus adding DD, each comprising a carboxylate and/or NE comprising a carboxylate and an amide is disclosed (see table 8). Attaching the entire peptide (except for the tyrosine being phosphorylated) to a tyrphostin reads on adding one or more specificity side chain elements to the combination of first and second modules. Methods for assaying (screening) for protein kinase inhibition are disclosed in columns 19-22. The reference also discloses other non-peptide molecules to which functional groups (i.e. first modules) may be covalently attached such as peptides with methylated amide linkages and those disclosed in the references cited in column 21, lines 49-55.

5. Claims 1, 3, 4, 6, 7, and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Dobrusin et al. US Patent 5,464,861 (November 1995).

The presently claimed invention is a method for identifying inhibitors of protein kinases including PDGF and EGF by attaching more than one functional group to an indole scaffold to form one or more combinations of functional groups and scaffold, at least one functional group being selected from hydroxy, carboxylic acid, and amide, and selecting combinations of functional groups and scaffold that inhibit protein kinase activity. At least one functional group is attached to the indole scaffold through a 1-3 carbon linear chain that is substituted with a N, O, or S.

The '861 patent discloses 137 indole derivatives in Table 1 that are tested for EGF and PDGF inhibition activity (see Table 2). Compound 92 comprises both hydroxyl and amide functional groups attached to the indole. Compound 23 comprises an amide linked to the indole

and a phenyl group linked to the indole through a S-CH_2 linkage (a 1-3 carbon chain substituted with a S.

Allowable Subject Matter

6. Claims 5 and 8 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

As allowable subject matter has been indicated, applicant's reply must either comply with all formal requirements or specifically traverse each requirement not complied with. See 37 CFR 1.111(b) and MPEP § 707.07(a).

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Tomas Friend** at telephone number **(703) 308-4548**. The examiner's normal schedule is four, ten-hour days per week including Saturdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-2742.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist at (703) 308-1235.

ANDREW WANG
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Tomas Friend, Ph.D.
22 January 2003